

## **Supplemental Material**

**Total RNA and DNA extraction.** RNA was extracted from frozen buffy coat previously obtained from 7.5 ml of whole blood using Ribopure Kit (Ambion), modified for miRNA extraction. Briefly, the buffy coat samples were separated within 30 minutes from the blood drawing, immediately snap frozen and subsequently stored at -80°C. Each thawed sample was mixed with 800 ul of Lyses Solution and 10 µl of glacial acetic acid. The sample was incubated in ice for 5 minutes and 500 µl of phenol-chlorophorm was added and vortexed vigorously to mix the phases. The sample was then centrifuged at 13000 rpm for 1-2 min to separate the phases and the aqueous phase was transferred to a new tube. 1 ml of Denaturation Solution and 2,7 ml of EtOH were added to the aqueous phase and transferred to a Filter Cartridge-Collection Tube connected to a vacuum system, washed with 700 µl of washing solution 1 (Denaturation solution + EtOH) and then with 700 µl of washing solution 2 (EtOH, NaCl 5M and RNase free water). The RNA was eluted in 150 µl of elution solution, quantified and stored at -80°C. Quantitative assessment of the RNA was performed using Nanodrop ND-1000 Biophotometer (NanoDrop Technologies): the lowest acceptable OD260/280 ratio was between 1.98 and 2.10. DNA was extracted using the Wizard Genomic DNA purification kit (Promega, Madison, WI, USA) following the manufacturer's instructions.

All laboratory analyses were done in the same batch, in samples that were never thawed until the analyses.

**Table S1.** miR-222, miR-21 and miR-146a expression by subjects' characteristics. The table is based on measurements taken after three consecutive days of work (time 2).

Variable	n	miR - 21			miR - 222			miR - 146		
		mean	95% CI	p-value <sup>a</sup>	mean	95% CI	p-value <sup>a</sup>	mean	95% CI	p-value <sup>a</sup>
<b>Age, years</b>										
< 39	21	5.13	(4.04; 6.22)		1.73	(0.36; 3.11)		0.94	(-1.00;2.87)	
39 - 47	21	4.66	(2.57; 6.75)		2.33	(1.08; 3.57)		2.89	(1.36; 4.43)	
> 47	21	4.09	(2.96; 5.21)	0.26	2.42	(1.53; 3.32)	0.37	2.21	(-1.13;5.55)	0.34
<b>Body Mass Index, Kg/m<sup>2</sup></b>										
< 25	21	4.00	(2.71; 5.29)		1.94	(1.02; 2.87)		4.14	(1.63; 6.65)	
25 -27.5	21	5.59	(4.54; 6.65)		1.81	(0.57; 3.04)		0.91	(-1.02;2.85)	
> 27.5	21	4.47	(2.68; 6.26)	0.58	2.70	(1.45; 3.94)	0.32	1.24	(-0.80;3.27)	0.08
<b>Number of cigarettes smoked per day</b>										
0	38	4.61	(3.45; 5.77)		2.34	(1.59; 3.09)		1.74	(0.09; 3.38)	
1-15	17	5.00	(3.70; 6.31)		1.89	(0.49; 3.30)		2.14	(-0.78;5.06)	
16 - 30	8	3.89	(4.61; 6.16)	0.84	1.97	(1.09; 5.04)	0.57	2.26	(-1.17;5.68)	0.74
<b>Duration of smoking, years</b>										
0	24	4.34	(2.81; 5.86)		2.09	(1.09; 3.08)		2.36	(0.53; 4.18)	
1-19	17	5.34	(4.06; 6.62)		2.18	(0.68; 3.67)		0.90	(-1.48;3.29)	
20-40	20	4.07	(2.74; 5.39)	0.88	2.38	(1.20; 3.56)	0.71	2.72	(-0.13;5.57)	0.86
<b>Duration of Employment, years</b>										
< 9	20	5.20	(3.92; 6.47)		2.93	(1.58; 4.27)		0.08	(-2.51;2.67)	
9 - 21	17	4.32	(2.89; 5.76)		0.65	(-0.63;1.93)		3.12	(0.63; 5.62)	
> 21	22	4.03	(2.32; 5.74)	0.24	2.86	(1.97; 3.75)	0.87	1.46	(-0.53;3.45)	0.41
<b>Education</b>										
Primary school	12	5.40	(3.94; 6.86)		2.99	(1.34; 4.64)		0.27	(-5.11;5.65)	
Middle school	37	4.92	(3.95; 5.90)		1.83	(1.01; 2.65)		2.11	(0.66; 3.55)	
High school	14	3.53	(1.42; 5.64)	0.09	2.50	(0.91; 4.08)	0.68	2.65	(0.15; 5.16)	0.26
<b>Area of residence</b>										
City centre	8	5.65	(3.75; 7.56)		1.87	(-0.49;4.23)		-0.60	(-4.5; 3.29)	
Suburbs	41	4.64	(3.65; 5.63)		2.21	(1.44; 2.97)		2.40	(0.82; 3.99)	
Rural	12	3.90	(1.96; 5.83)	0.24	2.23	(0.42; 4.04)	0.77	1.55	(-0.78;3.89)	0.47
<b>Self-reported traffic intensity near home</b>										
High	5	4.24	(-0.65; 9.13)		1.86	(-3.74;7.45)		0.14	(-6.35;6.63)	
Medium	38	4.85	(3.97; 5.73)		1.86	(1.05; 2.67)		2.40	(0.99; 3.80)	
Low	18	4.20	(1.95; 6.45)	0.76	2.83	(1.65; 4.01)	0.19	1.34	(-1.93;4.61)	0.95
<b>WBC, 10<sup>3</sup>/mm<sup>3</sup></b>										
4.0 - 5.9	14	5.24	(3.56; 6.91)		1.89	(0.77; 3.01)		1.75	(-0.49;3.98)	
5.9 -7.2	16	3.68	(1.45; 5.92)		1.63	(0.46; 2.81)		2.13	(-0.55;4.81)	
7.2 - 8.3	15	3.89	(2.2; 5.57)		3.28	(1.36; 5.19)		1.20	(-1.70;4.10)	
8.3 – 13.0	16	5.69	(4.47; 6.90)	0.58	2.09	(0.73; 3.46)	0.48	1.63	(-1.48;4.74)	0.81
<b>Granulocytes, %</b>										
44.6 - 52.4	14	4.30	(2.54; 6.06)		1.56	(0.31; 2.81)		1.56	(-1.45;4.57)	
52.4 - 58.1	15	4.84	(3.04; 6.64)		1.78	(0.51; 3.06)		2.83	(1.05; 4.62)	
58.1 - 62.4	16	4.76	(2.33; 7.18)		2.66	(0.67; 4.65)		0.41	(-3.0; 3.82)	
62.4 - 80.6	16	4.64	(3.32; 5.96)	0.84	2.49	(1.32; 3.65)	0.20	2.76	(0.13; 5.38)	0.83

<sup>a</sup>p - value test for trend

**Table S2.** Levels and distributions of estimated individual exposures to airborne Particulate Matter (PM) and PM metal components (n=63).

Exposure	Mean	SD	Min	Percentile			Max
				25 <sup>th</sup>	50 <sup>th</sup>	75 <sup>th</sup>	
PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	233.42	214.56	73.72	152.23	179.45	222.86	1220.17
PM <sub>1</sub> ( $\mu\text{g}/\text{m}^3$ )	8.48	6.18	1.71	3.51	9.01	11.35	30.49
Coarse ( $\mu\text{g}/\text{m}^3$ )	224.94	208.99	71.52	148.60	170.13	211.03	1189.69
Chromium ( $\mu\text{g}/\text{m}^3$ )	0.09	0.03	0.02	0.08	0.09	0.11	0.20
Lead ( $\mu\text{g}/\text{m}^3$ )	6.98	6.63	0.52	1.40	4.22	16.11	18.00
Cadmium ( $\mu\text{g}/\text{m}^3$ )	0.01	0.01	0.00	0.00	0.00	0.01	0.03
Arsenic ( $\mu\text{g}/\text{m}^3$ )	0.18	0.21	0.01	0.02	0.07	0.50	0.50
Nickel ( $\mu\text{g}/\text{m}^3$ )	0.43	0.26	0.10	0.24	0.34	0.62	0.90
Manganese ( $\mu\text{g}/\text{m}^3$ )	38.78	98.86	0.30	1.33	9.12	30.00	684.00

<sup>a</sup>Averages of the concentrations in the 11 work areas of the steel production facility weighted by the time spent in the areas by each of the study subjects.

Coarse particle concentrations were estimated as the difference between the concentrations of particulate matter with aerodynamic diameters <10  $\mu\text{m}$  (PM<sub>10</sub>) and <1  $\mu\text{m}$  (PM<sub>1</sub>). Metal components were measured in the PM<sub>10</sub> fraction of PM mass.

**Table S3.** Multivariable regression models (adjusted for age, body mass index, smoking, number of cigarettes/day, % granulocytes) estimating effects of Particulate Matter (PM) mass and PM metal component exposure on miR-222, miR-21 and miR-146a, according to smoking status (n=63).

		miR-222			miR-21			miR-146a		
	Exposure	$\beta_{std}$	95 CI %	p-value	$\beta_{std}$	95 CI %	p-value	$\beta_{std}$	95 CI %	p-value
<b>Non current smokers (n=38)</b>	$PM_{10}$	0.25	(-0.09; 0.59)	0.14	-0.20	(-0.65; 0.26)	0.38	-0.54	(-1.43; 0.36)	0.23
	$PM_1$	0.25	(-0.11; 0.62)	0.17	-0.25	(-0.75; 0.25)	0.31	0.16	(-0.45; 0.76)	0.59
	Coarse	0.25	(-0.09; 0.59)	0.14	-0.20	(-0.65; 0.26)	0.39	-0.57	(-1.48; 0.33)	0.20
	Chromium	0.56	(0.21; 0.92)	0.00	-0.23	(-0.77; 0.31)	0.39	-0.17	(-0.69; 0.36)	0.51
	Lead	0.55	(0.09; 1.00)	0.02	-0.17	(-0.87; 0.53)	0.61	-0.97	(-1.46; -0.49)	0.00
	Cadmium	0.42	(0.02; 0.83)	0.04	0.23	(-0.58; 1.04)	0.55	-0.71	(-1.24; -0.17)	0.01
	Arsenic	-0.07	(-0.68; 0.55)	0.82	-0.12	(-0.86; 0.63)	0.75	-0.35	(-1.03; 0.32)	0.29
	Nickel	0.29	(-0.39; 0.97)	0.38	-0.31	(-1.22; 0.61)	0.49	-0.12	(-0.91; 0.67)	0.76
	Manganese	0.55	(-0.38; 1.47)	0.23	0.73	(-0.76; 2.23)	0.32	0.48	(-0.65; 1.61)	0.39
<b>Current smokers (n=25)</b>	$PM_{10}$	0.06	(-0.44; 0.55)	0.82	0.06	(-0.32; 0.43)	0.76	-1.23	(-4.16; 1.7)	0.38
	$PM_1$	0.06	(-0.47; 0.6)	0.80	0.05	(-0.35; 0.46)	0.79	-0.06	(-1.17; 1.05)	0.91
	Coarse	0.05	(-0.44; 0.55)	0.82	0.06	(-0.32; 0.43)	0.76	-1.35	(-4.39; 1.69)	0.36
	Chromium	0.02	(-0.5; 0.53)	0.95	0.20	(-0.19; 0.59)	0.29	-0.16	(-0.61; 0.29)	0.45
	Lead	0.25	(-0.36; 0.85)	0.40	-0.03	(-0.52; 0.46)	0.90	-0.23	(-0.84; 0.38)	0.43
	Cadmium	-0.29	(-0.84; 0.26)	0.25	0.35	(-0.03; 0.73)	0.06	-0.16	(-0.53; 0.21)	0.32
	Arsenic	0.11	(-0.48; 0.7)	0.69	-0.13	(-0.6; 0.33)	0.55	-0.06	(-0.63; 0.52)	0.83
	Nickel	0.21	(-0.39; 0.81)	0.47	0.06	(-0.42; 0.55)	0.78	-0.26	(-0.84; 0.33)	0.36
	Manganese	-0.15	(-0.52; 0.22)	0.39	0.22	(-0.06; 0.5)	0.12	-0.09	(-0.44; 0.25)	0.58

**Table S4.** Multivariable regression models (adjusted for age, body mass index, smoking, number of cigarettes/day, % granulocytes) estimating effects of Particulate Matter (PM) mass and PM metal component exposure on miR-222, miR-21 and miR-146a, according to age (n=63).

		miR-222			miR-21			miR-146a		
	Exposure	$\beta_{std}$	95 CI %	p-value	$\beta_{std}$	95 CI %	p-value	$\beta_{std}$	95 CI %	p-value
<b>Age 25-44 years (n=33)</b>	$PM_{10}$	0.02	(-0.33; 0.27)	0.07	1.04	(-0.1; 2.18)	0.97	0.02	(-0.33; 0.27)	0.02
	$PM_1$	0.08	(-0.39; 0.27)	0.40	0.29	(-0.4; 0.98)	0.78	0.08	(-0.39; 0.27)	0.08
	Coarse	0.01	(-0.33; 0.27)	0.07	1.08	(-0.08; 2.24)	0.98	0.01	(-0.33; 0.27)	0.01
	Chromium	0.07	(-0.40; 0.33)	0.12	0.27	(-0.08; 0.63)	0.62	0.07	(-0.40; 0.33)	0.07
	Lead	-0.14	(-0.49; 0.35)	0.00	0.62	(0.23; 1.00)	0.46	-0.14	(-0.49; 0.35)	-0.14
	Cadmium	0.14	(-0.32; 0.69)	0.24	0.23	(-0.18; 0.63)	0.38	0.14	(-0.32; 0.69)	0.14
	Arsenic	-0.20	(-0.57; 0.36)	0.62	0.11	(-0.35; 0.58)	0.24	-0.20	(-0.57; 0.36)	-0.20
	Nickel	0.00	(-0.45; 0.45)	0.19	0.32	(-0.17; 0.81)	0.98	0.00	(-0.45; 0.45)	0.00
	Manganese	0.17	(-0.09; 0.63)	0.48	-0.12	(-0.47; 0.23)	0.18	0.17	(-0.09; 0.63)	0.17
<b>Age 45-60 years (n=30)</b>	$PM_{10}$	0.04	(-0.23; 0.31)	0.78	0.03	(-0.3; 0.36)	0.84	-0.71	(-2.03; 0.61)	0.27
	$PM_1$	0.04	(-0.27; 0.36)	0.78	0.01	(-0.39; 0.42)	0.95	-0.12	(-1.04; 0.8)	0.78
	Coarse	0.04	(-0.23; 0.31)	0.78	0.03	(-0.29; 0.36)	0.84	-0.74	(-2.07; 0.6)	0.26
	Chromium	0.30	(-0.36; 0.97)	0.34	-0.23	(-1.18; 0.71)	0.61	-0.56	(-1.66; 0.55)	0.29
	Lead	-0.27	(-0.96; 0.42)	0.42	-0.06	(-0.77; 0.65)	0.86	-0.06	(-1.02; 0.9)	0.89
	Cadmium	0.00	(-0.72; 0.73)	0.99	0.86	(-2.29; 4.01)	0.56	-0.67	(-1.61; 0.28)	0.15
	Arsenic	-0.24	(-0.98; 0.5)	0.50	-0.09	(-0.88; 0.69)	0.80	0.31	(-0.69; 1.3)	0.52
	Nickel	-0.18	(-0.83; 0.46)	0.56	-0.05	(-0.81; 0.7)	0.88	0.46	(-0.36; 1.28)	0.24
	Manganese	0.46	(-0.63; 1.55)	0.39	0.43	(-2.05; 2.91)	0.72	-0.07	(-1.73; 1.59)	0.93

**Table S5.** KEGG biological pathways potentially affected by miR-222, miR-21 and miR-146a.

Pathway	Target genes involved in the pathway		
	miR-222	miR-21	miR-146a
hsa00010 Glycolysis / Gluconeogenesis	5	2	3
hsa00020 Citrate cycle	2	2	1
hsa00030 Pentose phosphate pathway	2	1	1
hsa00040 Pentose and glucuronate interconversions	2	0	1
hsa00051 Fructose and mannose metabolism	2	1	1
hsa00052 Galactose metabolism	2	2	2
hsa00053 Ascorbate and aldarate metabolism	1	0	0
hsa00061 Fatty acid biosynthesis	0	0	1
hsa00062 Fatty acid elongation in mitochondria	0	0	1
hsa00071 Fatty acid metabolism	2	3	3
hsa00072 Synthesis and degradation of ketone bodies	0	1	1
hsa00100 Steroid biosynthesis	0	2	2
hsa00120 Primary bile acid biosynthesis	0	1	1
hsa00140 C21-Steroid hormone metabolism	0	0	1
hsa00150 Androgen and estrogen metabolism	1	1	1
hsa00190 Oxidative phosphorylation	3	0	6
hsa00230 Purine metabolism	10	4	12
hsa00232 Caffeine metabolism	0	0	1
hsa00240 Pyrimidine metabolism	2	2	10
hsa00250 Alanine, aspartate and glutamate metabolism	3	1	0
hsa00260 Glycine, serine and threonine metabolism	0	2	1
hsa00270 Cysteine and methionine metabolism	4	1	2
hsa00280 Valine, leucine and isoleucine degradation	1	1	4
hsa00290 Valine, leucine and isoleucine biosynthesis	1	1	2
hsa00310 Lysine degradation	1	3	1
hsa00330 Arginine and proline metabolism	2	3	0

Pathway	Target genes involved in the pathway		
	miR-222	miR-21	miR-146a
hsa00340 Histidine metabolism	1	2	1
hsa00350 Tyrosine metabolism	1	1	1
hsa00360 Phenylalanine metabolism	0	1	1
hsa00380 Tryptophan metabolism	1	1	0
hsa00430 Taurine and hypotaurine metabolism	1	0	0
hsa00410 beta-Alanine metabolism	0	1	0
hsa00450 Selenoamino acid metabolism	0	1	0
hsa00460 Cyanoamino acid metabolism	0	1	0
hsa00472 D-Arginine and D-ornithine metabolism	0	1	0
hsa00480 Glutathione metabolism	4	4	2
hsa00500 Starch and sucrose metabolism	3	3	3
hsa00510 N-Glycan biosynthesis	1	2	0
hsa00512 O-Glycan biosynthesis	1	0	0
hsa00511 Other glycan degradation	0	1	0
hsa00512 O-Glycan biosynthesis	0	2	0
hsa00520 Amino sugar and nucleotide sugar metabolism	2	1	2
hsa00531 Glycosaminoglycan degradation	0	1	0
hsa00532 Chondroitin sulfate biosynthesis	1	0	1
hsa00533 Keratan sulfate biosynthesis	0	1	2
hsa00534 Heparan sulfate biosynthesis	1	2	2
hsa00561 Glycerolipid metabolism	3	0	1
hsa00562 Inositol phosphate metabolism	3	2	2
hsa00563 Glycosylphosphatidylinositol	1	0	2
hsa00564 Glycerophospholipid metabolism	4	2	5
hsa00565 Ether lipid metabolism	2	1	2
hsa00590 Arachidonic acid metabolism	3	2	4
hsa00591 Linoleic acid metabolism	0	1	3
hsa00592 alpha-Linolenic acid metabolism	1	1	2

Pathway	Target genes involved in the pathway		
	miR-222	miR-21	miR-146a
hsa00600 Sphingolipid metabolism	4	0	1
hsa00601 Glycosphingolipid biosynthesis - lacto and neolacto series	1	1	3
hsa00603 Glycosphingolipid biosynthesis - globo series	2	1	0
hsa00604 Glycosphingolipid biosynthesis - ganglio series	1	1	0
hsa00620 Pyruvate metabolism	6	3	3
hsa00640 Propanoate metabolism	1	2	1
hsa00650 Butanoate metabolism	1	2	2
hsa00740 Riboflavin metabolism	1	1	1
hsa00750 Vitamin B6 metabolism	0	1	0
hsa00760 Nicotinate and nicotinamide metabolism	0	1	2
hsa00770 Pantothenate and CoA biosynthesis	1	0	3
hsa00780 Biotin metabolism	0	0	1
hsa00830 Retinol metabolism	4	2	5
hsa00860 Porphyrin and chlorophyll metabolism	2	1	2
hsa00900 Terpenoid backbone biosynthesis	3	0	1
hsa00903 Limonene and pinene degradation	0	1	1
hsa00910 Nitrogen metabolism	1	1	1
hsa00970 Aminoacyl-tRNA biosynthesis	1	1	2
hsa00980 Metabolism of xenobiotics by cytochrome P450	2	2	3
hsa00982 Drug metabolism - cytochrome P450	1	1	4
hsa00983 Drug metabolism - other enzymes	1	1	3
hsa01040 Biosynthesis of unsaturated fatty acids	0	0	1
hsa01100 Metabolic pathways	48	27	61
hsa02010 ABC transporters	4	1	3
hsa03010 Ribosome	2	3	4
hsa03018 RNA degradation	2	4	3
hsa03020 RNA polymerase	1	0	2
hsa03022 Basal transcription factors	1	3	3

Pathway	Target genes involved in the pathway		
	miR-222	miR-21	miR-146a
hsa03030 DNA replication	1	1	1
hsa03050 Proteasome	3	1	4
hsa03060 Protein export	0	3	1
hsa03320 PPAR signaling pathway	4	4	4
hsa03410 Base excision repair	3	0	3
hsa03420 Nucleotide excision repair	2	2	4
hsa03430 Mismatch repair	1	2	0
hsa03440 Homologous recombination	1	1	2
hsa03450 Non-homologous end-joining	2	0	0
hsa04010 MAPK signaling pathway	14	11	9
hsa04012 ErbB signaling pathway	4	3	3
hsa04020 Calcium signaling pathway	7	4	8
hsa04060 Cytokine-cytokine receptor interaction	7	17	14
hsa04062 Chemokine signaling pathway	10	9	10
hsa04070 Phosphatidylinositol signaling system	5	1	3
hsa04080 Neuroactive ligand-receptor interaction	10	9	7
hsa04110 Cell cycle	7	7	5
hsa04115 p53 signaling pathway	2	4	4
hsa04120 Ubiquitin mediated proteolysis	8	4	4
hsa04130 SNARE interactions in vesicular transport	0	0	1
hsa04140 Regulation of autophagy	1	2	0
hsa04142 Lysosome	6	2	3
hsa04144 Endocytosis	0	5	5
hsa04150 mTOR signaling pathway	7	1	1
hsa04210 Apoptosis	6	3	6
hsa04260 Cardiac muscle contraction	3	2	1
hsa04270 Vascular smooth muscle contraction	6	7	6
hsa04310 Wnt signaling pathway	10	5	4

Pathway	Target genes involved in the pathway		
	miR-222	miR-21	miR-146a
hsa04320 Dorso-ventral axis formation	1	3	2
hsa04330 Notch signaling pathway	2	2	1
hsa04340 Hedgehog signaling pathway	2	2	2
hsa04350 TGF-beta signaling pathway	3	4	5
hsa04360 Axon guidance	8	5	3
hsa04370 VEGF signaling pathway	1	2	3
hsa04510 Focal adhesion	7	8	10
hsa04512 ECM-receptor interaction	2	1	4
hsa04514 Cell adhesion molecules	4	3	1
hsa04520 Adherens junction	4	1	4
hsa04530 Tight junction	7	0	7
hsa04540 Gap junction	4	1	4
hsa04610 Complement and coagulation cascades	3	5	3
hsa04612 Antigen processing and presentation	3	4	3
hsa04620 Toll-like receptor signaling pathway	5	3	7
hsa04621 NOD-like receptor signaling pathway	4	2	1
hsa04622 RIG-I-like receptor signaling pathway	5	2	3
hsa04630 Jak-STAT signaling pathway	3	13	5
hsa04640 Hematopoietic cell lineage	3	6	3
hsa04650 Natural killer cell mediated cytotoxicity	4	8	7
hsa04660 T cell receptor signaling pathway	6	5	3
hsa04662 B cell receptor signaling pathway	5	5	3
hsa04664 Fc epsilon RI signaling pathway	3	4	4
hsa04666 Fc gamma R-mediated phagocytosis	2	1	3
hsa04670 Leukocyte transendothelial migration	6	1	5
hsa04710 Circadian rhythm - mammal	1	0	2
hsa04720 Long-term potentiation	4	2	2
hsa04722 Neurotrophin signaling pathway	9	5	3

Pathway	Target genes involved in the pathway		
	miR-222	miR-21	miR-146a
hsa04730 Long-term depression	3	1	4
hsa04740 Olfactory transduction	6	9	13
hsa04742 Taste transduction	1	1	1
hsa04810 Regulation of actin cytoskeleton	9	9	12
hsa04910 Insulin signaling pathway	7	10	6
hsa04912 GnRH signaling pathway	4	3	4
hsa04914 Progesterone-mediated oocyte maturation	6	6	4
hsa04916 Melanogenesis	5	1	2
hsa04920 Adipocytokine signaling pathway	4	2	3
hsa04930 Type II diabetes mellitus	6	1	1
hsa04940 Type I diabetes mellitus	1	3	1
hsa04950 Maternity onset diabetes of the young	1	0	0
hsa05010 Alzheimer's disease	5	0	6
hsa05012 Parkinson's disease	5	3	5
hsa05014 Amyotrophic lateral sclerosis	5	1	1
hsa05016 Huntington's disease	6	1	9
hsa05020 Prion diseases	2	0	1
hsa05110 Vibrio cholerae infection		0	2
hsa05120 Epithelial cell signaling in Helicobacter pylori infection	4	1	3
hsa05130 Pathogenic Escherichia coli infection	2	1	4
hsa05200 Pathways in cancer	18	12	19
hsa05210 Colorectal cancer	6	3	5
hsa05211 Renal cell carcinoma	1	2	2
hsa05212 Pancreatic cancer	3	1	4
hsa05213 Endometrial cancer	3	1	3
hsa05214 Glioma	2	2	4
hsa05215 Prostate cancer	6	1	5
hsa05216 Thyroid cancer	2	0	0

Pathway	Target genes involved in the pathway		
	miR-222	miR-21	miR-146a
hsa05217 Basal cell carcinoma	3	2	1
hsa05218 Melanoma	1	2	4
hsa05219 Bladder cancer	2	1	2
hsa05220 Chronic myeloid leukemia	6	2	3
hsa05221 Acute myeloid leukemia	6	2	6
hsa05222 Small cell lung cancer	4	1	7
hsa05223 Non-small cell lung cancer	1	1	3
hsa05310 Asthma	0	1	2
hsa05320 Autoimmune thyroid disease	1	2	3
hsa05322 Systemic lupus erythematosus	5	4	2
hsa05330 Allograft rejection	1	3	2
hsa05332 Graft-versus-host disease	2	2	2
hsa05340 Primary immunodeficiency	2	3	3
hsa05410 Hypertrophic cardiomyopathy	0	2	1
hsa05412 Arrhythmogenic right ventricular cardiomyopathy	3	1	2
hsa05414 Dilated cardiomyopathy	2	1	1